JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 65, NO. 18, 2015

ISSN 0735-1097/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jacc.2015.03.516

EDITORIAL COMMENT

The Dawn of a Better Day for Patients With Hypertrophic Cardiomyopathy*

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Hypertrophic cardiomyopathy (HCM) was initially described as an uncommon and largely untreatable disorder, a view derived from small cohorts of highly selected and severely symptomatic patients evaluated at major HCM referral centers many decades ago (1,2). This misleading perception of HCM persists among many clinicians and is often reinforced in patients by contradictory information derived from social media and the Internet. HCM patients deserve better. The reality is that in barely 1 generation of investigators, this disease has evolved from a grim and largely untreatable condition to a treatable disorder associated with a normal or nearly normal life expectancy in most patients. This remarkable result has been achieved by a more balanced understanding of the natural history of HCM in less selected patient populations (3,4) and through major advances in cardiovascular therapy, including implantable cardioverter-defibrillators (ICDs) for primary prevention of sudden death, surgical septal myectomy for relief of progressive heart failure symptoms in patients with left ventricle (LV) outflow obstruction, and transplantation and other supportive mechanical therapies in the minority of non-obstructive cardiac disease patients with advanced heart failure unresponsive to pharmacologic treatment (5–12).

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In this issue of the *Journal*, Maron et al. (13) report the clinical course of 1,000 consecutive adult patients with HCM evaluated at 2 HCM referral centers over a period of 20 years. Mean follow-up was 7 years, with detailed records obtained in 98% of study patients. Appropriate ICD interventions, heart transplantation, and out-of-hospital resuscitation from cardiac arrest prevented deaths in 56 of the study patients. Of the 258 patients who underwent septal reduction therapy (surgical myectomy in most), 90% were alive almost 10 years after the procedure, most with mild or no symptoms. Only 40 study patients died of HCM-related causes during follow-up. Of these patients, 17 died suddenly, 12 because they either declined ICD implantation or were evaluated in the 1990s, before the ICD had become part of HCM management; 4 others did not have implants because they did not have major conventional risk factors; and 1 had an ICD known to malfunction by the manufacturer, an extensively reported clinical case (14). It is fair to assume that these patients would not have died suddenly if they had had an ICD. Of the remaining 23 patients whose deaths were HCM-related, 17 died of advanced heart failure (with or without heart transplants) in the absence of LV outflow obstruction. Therefore, the dominant cause of HCM-related mortality in this large consecutive cohort changed from sudden and unexpected death to death due to advanced heart failure.

Results of this study show what contemporary management in a referral HCM population can achieve. The rate of HCM-related death was 0.5%/year, an event rate well below that reported decades ago for this disease and not different from that of the general U.S. population (13). This event rate could serve as a target for HCM management. These findings also show that the greatest challenge in the management of patients with HCM is gradually shifting from prevention of sudden death as the predominant threat to the management of heart failure symptoms in the absence of LV outflow obstruction. This is a major step forward in treating a disease in which most instances of sudden deaths occur in young and asymptomatic patients who have the expectation of many years of

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

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rewarding life and deserve this aspiration to be fulfilled by modern cardiovascular medicine.

Do we now have all the answers to manage the risk of sudden death in HCM? Without doubt, many HCM patients worldwide are still alive today because of the ICD. However, do all HCM patients who have received ICD implants definitely need the device? This question is not confined to this disorder; it is clearly a problem with risk stratification for sudden death in cardiovascular disease and coronary artery disease, other cardiomyopathies and arrhythmogenic genetic diseases alike. In the present study by Maron at al. (13), the ratio of the total number of implanted ICDs to devices that intervened appropriately during follow-up was 9:1, not substantially different from that in large randomized trials of patients with LV systolic dysfunction and congestive heart failure due to ischemic or nonischemic causes (15). This 9:1 ratio is probably higher than we would like and can be largely explained by the persisting uncertainties in risk stratification for individual patients with HCM (16,17). An equally valid question is what ratio would we consider acceptable? It is unrealistic to expect that we will ever arrive at a 4:1 or 3:1 ratio, and we will never reach a 1:1 ratio. In HCM, the extreme disease heterogeneity and relatively low absolute number of sudden deaths constitute impediments to achieving such goals. Furthermore, due to these difficulties in risk stratification, the decision of whether to implant an ICD often requires an open discussion with the patient about the benefits and potential complications of the device, as well as the strength of the available evidence for risk assessment (18). Therefore, the individual patient's personal and psychological attitude toward the risk of sudden death contributes to the final decision and the number of implanted ICDs, a number also influenced by problems of legal liability perceived by clinicians. However, several positive aspects of this complex issue must be kept in mind. As the result of better contemporary ICD programming, improved technology, and more experienced electrophysiologists, inappropriate shock rates are now much lower. Another important aspect not generally addressed in published reports is the psychological benefit that patients derive from being relieved from the constant fear of sudden death, a feeling fully appreciated only by those who have been exposed to the unpredictable risk of this event.

In conclusion, as shown by Maron et al. (13), contemporary treatments can fulfill the expectations of many patients with HCM by effectively preventing sudden death, extending life expectancy, and improving quality of life in a complex genetic disease associated, in this cohort, with a low mortality not dissimilar from that of the general population.

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KEY WORDS heart failure, life expectancy, sudden death